OPTOGENETICS AS A NEW PARADIGM FOR DYNAMIC CONTROL IN METABOLIC ENGINEERING

José L. Avalos, Princeton University, USA
javalos@princeton.edu
Jared Toettcher, Princeton University, USA
Evan Zhao, Princeton University, USA

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We recently developed optogenetic circuits to control engineered metabolic pathways for microbial chemical production with light[1]. Light offers unique capabilities for dynamic control of fermentation processes. It is highly tunable and can be applied or removed instantly, and in any desired schedule, to elicit reversible metabolic responses without chemical inducers or complex media changes. In this talk, I will present our recent progress in the development of this new technological platform. I will describe new optogenetic circuit designs that enhance the transcriptional activation kinetics of inverter (OptoINVRT) circuits upon exposure to darkness, which improve the robustness of light-controlled cell growth and chemical production. In addition, I will introduce a new class of optogenetic circuits for metabolic engineering (OptoAMP), which amplify the transcriptional response to light, enabling strong light-induced gene expression in high cell-density fermentations in lab-scale bioreactors of up to five liters. Furthermore, I will present new optogenetic post-translational controls based on light-dependent assembly of synthetic organelles, which we use to control flux through branched metabolic pathways. I will demonstrate how each of these technologies can be applied to dynamically control engineered metabolisms to boost yields, titers, productivities, and product specificities of fuels and chemicals in microbial fermentations. Finally, I will provide a perspective on how optogenetics may emerge as a new paradigm for dynamic control in metabolic engineering.

1. Zhao EM, Zhang Y, Mehl J, Park H, Toettcher JE*, Avalos JL*. Optogenetic regulation of engineered cellular metabolism for microbial chemical production. *Nature* 29; 555 (7698):683-87 (2018). * Co-corresponding.